

AMENDMENTS TO THE SPECIFICATION

Please insert the attached "Sequence Listing" (pages 139 through 202), and comprising SEQ ID NOS: 1 -76, into the above-referenced application.

On page four, line number 13 please amend as follows:

Figures 1A-~~1H~~ 1G present topology of the MurI fold and various conformations of the enzyme. Figure 1A illustrates the three dimensional structure of one domain of MurI depicting structural elements and illustrates the topology of the MurI fold. Figures 1B and 1C provide a cartoon depiction of MurI in an open (1B; black) and closed (1C; gray) conformations. Figures 1D and 1F depict the tail-tail structure of Gram positive MurI in different conformations. Figure 1E depicts the head-head structure of atypical MurI. Figure 1G depicts the structure of Gram negative MurI having both a substrate binding site (left side of 1G) and an activator binding site (right side of 1G).

On page 36, line numbers 22 and 23 please amend as follows:

The coordinates determined represent those of MurI alone, and MurI in complex with the substrate (L-glutamate), in complex with activator (UDP-MurNAc-Ala), and in complex with substrate (L-glutamate) and activator (UDP-MurNAc-Ala). Crystallization of *E. coli* MurI is described in Example 2 and Figures 8-11. Results show that the unit of the crystal consists of one molecule corresponding to a monomer; the native form of MurI from Gram negative bacteria is a monomer. The monomer has two domains, which both have similar alpha/beta type folds. The binding of the substrate clearly identifies the binding site that is situated between the two domains (~~See left side of Figure 1H~~). The activator, UDP-MurNAc-Ala, binds at the opposite side of the protein (~~See right side of Figure 1H~~), possibly acting as a modulator of activity by inducing the correct conformation of the binding site by modulation of the relative position of the two domains of the protein. Thus, the hinge region located between the two domains is flexible such that when activator is bound, the conformation of the protein changes at the hinge region to make the substrate binding site available.

On page 41, line number 18, please amend as follows:

As described in the examples that follow, MurI of *E. faecalis*, *S. aureus*, and *E. faecium* have been crystallized and the crystal structure (three-dimensional structure) of each determined. The structures determined represent that of MurI alone, in complex with the enzyme product (substrate), such as D-glutamate or L-glutamate, or in complex with an inhibitor. Crystallization of *E. faecalis*, *E. faecium*, and *S. aureus* MurI is described in Examples 3-5, and Figures 12-18. Results show that the asymmetric unit of the crystal consists of a dimer which can exist in symmetrical (see Figure 1G) or non-symmetrical forms (see Figure 1H), depending on whether one or both of the substrate binding sites are occupied or open. The MurI protein is a four-domain structure in terms of overall folding; each domain has folds of the alpha/beta type. The molecular interface of Gram positive bacterium exists between two of the domains and functions as a flexible element by which a change in conformation opens the substrate binding site, allowing substrate to bind MurI.